

### Remarks

Claims 1, 3-6 and 8-11 are pending. Claims 12 and 13 are cancelled herein. Claim 11 has been amended to overcome a claim objection.

#### Claim Objections

The Examiner has objected to Claim 11 as having "SEQ ID No:" typed instead of "SEQ ID NO:". Claim 11 has been amended accordingly. Applicants appreciate the Examiner pointing out the typographical error.

#### Section 112, first paragraph, Rejection (Enablement)

The Examiner has maintained the rejection of Claims 12 and 13 under 35 U.S.C. §112, first paragraph, as being non-enabled. As Claims 12 and 13 have been cancelled herein, Applicants respectfully submit that this rejection is obviated.

#### Section 102 Rejections

The Examiner rejected claims 1, 3-6 and 9-11 under 35 U.S.C. §102(b) as being anticipated by WO 98/12345 ("Politino (A)"). The Examiner alleges that Politino (A) teaches a method for producing desacetylcephalosporin C using a cephalosporin esterase for *Rhodospiridium toruloides* (Example 2). This rejection is respectfully traversed.

Applicants have thoroughly read Politino (A) and respectfully submit that the Examiner's reliance on Politino (A) is misplaced. Politino (A) describes the cloning and sequencing of *R. toruloides* cephalosporin esterase genomic and cDNA genes. It does not, however, describe the direct fermentation of desacetylcephalosporin C by expression of the cephalosporin esterase gene in *A. chrysogenum*, as in the present invention. The sections of Politino (A) relied on by the Examiner merely show the characterization of the cephalosporin esterase so produced.

Specifically, in Example 2, the esterase enzyme is added to a reaction mixture containing cephalosporin (emphasis added). A by-product of that reaction was desacetyl cephalosporin C, evidencing the efficacy of the recombinantly produced enzyme. This is not relevant, however, to a discussion of the present invention which involves a recombinant fungal organism capable of directly fermenting desacetylcephalosporin C. The Examiner has not provided a reference showing a process for the direct production of desacetylcephalosporin C which comprises culturing a strain of *Acremonium chrysogenum* that contains (1) nucleic acid encoding enzymes for cephalosporin C biosynthesis and (2) a recombinant nucleic acid encoding *Rhodospiridium* cephalosporin esterase, under the stated conditions.

Turning to the Examiner's rejection in detail, the Examiner points to Example 2 in Politino (A) and states that desacetylcephalosporin C is produced by transforming *C. acremonium* (a.k.a. *A. chrysogenum*) with DNA encoding R. esterase. The Examiner goes on to state that *A. chrysogenum* is "producing cephalosporin C and contains nucleic acid encoding enzymes for cephalosporin C biosynthesis and recombinant nucleic acid encoding R. esterase" and concludes that this anticipates the present invention. However, this is not Applicants' invention. Rather, Applicants' invention is a process for the direct production of desacetylcephalosporin C using a single recombinant organism which produces both cephalosporin C and cephalosporin esterase. In Example 2 of Politino (A), the recombinantly produced enzyme is added to cephalosporin (Column 9, line 60) in order to characterize the enzyme. There simply is no direct production of desacetylcephalosporin C using a single organism in the manner set forth in the present invention. Accordingly, Politino (A) does not teach or suggest the elements of the claimed invention and is therefore not a proper reference under Section 102.

The Examiner has also rejected Claims 1, 3-6 and 9-11 under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 5,869,309 ("Politino (B)"). Politino (B) is the U.S. counterpart of Politino (A) which is a PCT application and contains the same teachings. Accordingly, for the same reasons set forth above, Applicants respectfully submit that Politino (B) does not teach or suggest the element of the claimed invention and is therefore not a proper reference under Section 102.

For these reasons, Applicants respectfully submit that withdrawal of the rejections under Section 102 is appropriate and is respectfully requested.

#### Section 103 Rejection

The Examiner has rejected Claim 8 under 35 U.S.C. §103(a) as being unpatentable over Politino (A) or (B) in view of U.S. Patent No. 4,533,632 ("Smith"). The Examiner alleges that Smith teaches a process for the preparation of desacetylcephalosporin C by fermenting *Acremonium chrysogenum* in the presence of esterase from *Rhodospiridium toruloides*. The process of fermentation is carried out at 15°-45° C and pH 4-9. The Examiner alleges that it would have been obvious at the time of the present invention to use *Acremonium chrysogenum* transformed with a DNA encoding *Rhodospiridium toruloides* esterase in the production of desacetylcephalosporin C.

The Examiner has only made conclusory statements without providing the requisite motivation necessary for a proper rejection under Section 103. Nonetheless, the deficiencies of Politino (A) and (B) noted above cannot, of course, be remedied by the teachings of Smith.

Accordingly, Applicants respectfully submit that withdrawal of the rejection under Section 103 is appropriate and is respectfully requested.

Conclusion

In view of the amendments and remarks above, Applicants submit that the claims are in condition for allowance and favorable action is therefore respectfully requested.

Please direct any questions regarding this reply to the undersigned attorney.

Respectfully submitted,

Bristol-Myers Squibb Company  
Patent Department  
P.O. Box 4000  
Princeton, NJ 08543-4000  
(609) 252-3883

  
Keith R. Lange  
Attorney for Applicants  
Reg. No. 44,201

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